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Accommodation-Induced Changes in Iris Curvature

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Abstract

Eyes were imaged using anterior segment ultrasound biomicroscopy to compare alterations in iris contour following the onset of accommodation in eyes with narrow angles, pigment dispersion syndrome, and controls. A radial perpendicular image in the horizontal temporal meridian was obtained for one eye while the subject focused on a distant target (~6m, unaccommodated state) with the fellow eye. The subject then focused steadily on a near target (~0.33m, accommodated state) for three minutes. Images were acquired at 0, 1, 2, and 3 minutes. Iris curvature was determined by measuring the maximum distance between the posterior iris surface and a line from the iris root to the first point of contact between the iris and lens. In control subjects (n = 22), iris curvature decreased immediately after the onset of accommodation, but not significantly (p = 0.49), from $246 \pm 37 \mu\text{m}$ (mean $\pm$ SEM) to $205 \pm 82 \mu\text{m}$; curvature increased after three minutes of accommodation to $298 \pm 57 \mu\text{m}$ (p = 0.10 vs. onset of accommodation). Eyes with pigment dispersion syndrome (n = 15) exhibited curvatures of $60 \pm 79 \mu\text{m}$ when unaccommodated, $-3 \pm 83 \mu\text{m}$ immediately after accommodation (p = 0.12), and $146 \pm 94 \mu\text{m}$ (p = 0.01) three minutes later. Eyes with narrow angles (n = 16) exhibited curvatures of $449 \pm 45 \mu\text{m}$ when unaccommodated, $414 \pm 46 \mu\text{m}$ immediately after accommodation (p = 0.37), and $523 \pm 40 \mu\text{m}$ (p < 0.01) three minutes later. The results confirm the time-dependent nature of iris contour response, with significant differences observed between the initial observation after accommodation and the observation three minutes later. The largest drop in curvature immediately after accommodation and the most rapid increase in curvature during subsequent observation were seen in the PDS subjects. We suspect that the more rapid increase in curvature in the PDS subjects is due to the elevated anterior-chamber pressure caused by the "reverse pupillary block" effect.

Keywords

pigment dispersion syndrome; pigmentary glaucoma; reverse pupillary block; aqueous humor

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Introduction

Although the most important consequence of accommodation is a change in focal distance, the mechanical consequences of accommodation are also important. Accommodation leads to posterior bowing of the iris, particularly in patients with pigment dispersion syndrome (PDS) (Pavlin et al. 1994; Pavlin et al. 1996). Iris bowing is largely eliminated in patients with PDS after a peripheral iridotomy when observed with ultrasound biomicroscopy (UBM) (Pavlin et al. 1996). Normal subjects show a posterior shift in iris contour with accommodation (Liebmann et al. 1995; McWhae et al. 1996; Ueda et al. 1997). Older patients show a pronounced decrease in posterior bowing following accommodation (Adam et al. 2004), consistent with the reduced lens motion of presbyopia. These results are all consistent with the "reverse pupillary block" hypothesis as applied to accommodation: anterior motion of the central lens pushes aqueous humor toward the peripheral posterior chamber, but the iris is pinned against the lens and blocks the flow (Karickhoff 1992).

None of these studies, however, examined iris contour changes over time, reporting only "before" and "after" configurations. Computational studies suggest that the dynamic response is important, and that after an initial large deflection, the iris contour should recover over the next three to five minutes (Heys et al. 2002; Huang et al. 2006). The essential hypothesis to be tested in this study was that the iris would exhibit posterior curvature immediately following accommodation, then recover to a more anterior curvature during the subsequent minutes. It was further hypothesized that pigment-dispersion patients, who exhibit strong posterior curvatures, would have more pronounced initial changes and slower recoveries than normal or narrow-angle patients, since a slower recovery would be consistent with chronic posterior curvature.

Methods

The study protocol was approved by the Institutional Review Board (IRB) for Human Research of the New York Eye and Ear Infirmary, and informed consent was obtained; the study adhered to the Declaration of Helsinki. After a complete eye exam including slit-lamp biomicroscopy, IOP measurement, gonioscopy and stereoscopic optic disc examination, three subject groups were recruited for the study (Table 1):

- Group 1 (Anatomic narrow angles (ANA), n=16): Subjects who had Shaffer grade two or less angles in the sitting position by 4-mirror gonioscopy without pressure on the cornea, without a double-hump sign on indentation gonioscopy in the dark and no peripheral anterior synechiae. ANA is most common in older females, and the make-up of this group represents the general trend of ANA patients. The ANA group was included to provide the maximum possible contrast with the PDS group (i.e., narrow angles and anterior iris curvature vs. open angles and posterior iris curvature).
- Group 2 (PDS, n=15): A diagnosis was made by the presence of a Krukenberg spindle, midperipheral, radial, iris transillumination defects, and moderate to dense homogeneous trabecular meshwork pigmentation on gonioscopy, irrespective of elevated intraocular pressure with or without glaucomatous damage. In contrast to ANA, PDS is most common in young males, again represented demographically by the sample group.
- Group 3 (controls, n=22): Subjects who had no ocular disease apart from refractive error. Controls were selected to match the PDS group (#3) with respect to age and refractive error, making them necessarily younger than the ANA group (#1). Rather than gender-match either group, we chose to take controls of both genders.

Patients were excluded if they had any ocular pathology that could lead to posterior synechiae, such as history of active uveitis, miotic therapy, or exfoliation syndrome. Subjects were excluded if they had undergone previous incisional or laser surgery, or if they had used topical medications affecting pupillary diameter.

All subjects underwent UBM (Ultrasound Biomicroscope Model P40 UBM; Paradigm Medical Industries Inc, Salt Lake City, UT) examination to assess accommodation-induced changes in iris curvature. UBM was performed in the supine position (Figure 1) using an immersion technique and a 50 MHz transducer that provides 4 to 5 mm of tissue penetration and provides lateral and axial resolution of approximately 50 μm and 25 μm , respectively. The scanner produces a 5×5 mm field with 256 vertical image lines (or A-scans) at a scan rate of 8 frames per second.

First, the subject was instructed to focus on a target at a distance of ~ 6 m (unaccommodated state) with the left eye under standard room lighting conditions (Figure 1b). A radial perpendicular image in the horizontal temporal meridian detailing the iris configuration was obtained for the right eye. During the examination, if the subject was not able to see the distant target, the left eye was given full refractive correction (contact lenses). The subject was then instructed to focus on a near (~ 0.33 m) target (accommodated state, Figure 1c) and to continue focusing on the same target for three minutes. Images were acquired at 0, 1, 2, and 3 minutes. While imaging the patients' eye with UBM, the operator continuously monitored the patient's eye movements to ensure that accommodation was maintained, as a change in the patient's focus would be easily identified. Patients who failed to maintain the fixation were not included in the study. Images were ported to the NIH image-analysis program *ImageJ*, and iris curvature was determined.

The iris curvature was calculated by drawing a line connecting the most peripheral and most central points of the iris pigment epithelium, and then measuring the largest perpendicular distance (anterior/convex = positive, posterior/concave = negative) from the line to the iris pigment epithelium (Liebmann et al. 1994; Liebmann et al. 1995).

Population averages are reported as mean $\pm$ SEM. Statistical significance of changes in curvature was assessed via a two-tailed paired t-test. Results were considered significant if $p < 0.05$ (i.e., 95% confidence).

Results

Representative UBM images of patients from each group are shown in Figure 3, and curvature data are presented in summary form in the bar graph of Figure 4. The iris curvature decreased immediately following accommodation in 13 of 22 control subjects (59%). As can be seen in Figure 2, the average curvature over the control group decreased from 246 ± 37 μm (mean $\pm$ SEM) to 205 ± 82 μm ($p = 0.49$). Three minutes after accommodation, the curvature increased in 16 of 22 subjects (73%). The final curvature, 298 ± 57 μm , was higher than that immediately after accommodation ($p = 0.10$), and higher than that in the unaccommodated state ($p = 0.15$), but neither result was significant at the 95% confidence level.

For the ANA group, curvature decreased immediately following accommodation in 9 of 16 eyes (53%). The average curvature decreased from 449 ± 45 μm to 414 ± 46 μm ($p = 0.37$). Given that the average age of the group was 55, it is unlikely that much accommodation was possible for most of the subjects. Over the following three minutes, the curvature increased in 12 of 16 subjects (75%), to a final value of 523 ± 40 μm , significantly higher than that immediately after accommodation ($p = 0.01$) and that in the unaccommodated state ($p = 0.02$).

For the PDS group, curvature decreased immediately after accommodation in 9 of 15 eyes (60%). The average curvature decreased from $60 \pm 79 \mu\text{m}$ to $-3 \pm 83 \mu\text{m}$ ($p = 0.12$). Over the following three minutes, the curvature increased in 11 of 15 subjects (73%), to a final value of $146 \pm 94 \mu\text{m}$, significantly higher than that immediately after accommodation ($p = 0.01$) and that in the unaccommodated state ($p = 0.04$). In contrast to previous observations (Adam et al. 2004), the change in curvature immediately following accommodation (i.e., from unaccommodated to accommodated+0 min) was not significantly correlated with age for any group ($R^2 = 0.033$, $p > 0.2$).

Figure 5 shows the average curvature values as a function of time following accommodation. Linear regression of the points gave a small rise for the control and ANA groups ($p = 0.17$ and 0.13 , respectively, for the null hypothesis of zero slope), but the PDS group gave a highly significant response ($p = 0.01$). As can be seen in the plot, the slope of the best-fit line is higher for the PDS subjects ($49.5 \mu\text{m}/\text{min}$) than for the control ($25.4 \mu\text{m}/\text{min}$) and ANA ($30.8 \mu\text{m}/\text{min}$) groups. The difference between the slope for the PDS group and the others was not significant at the 95% level ($p = 0.19$ and 0.24 with for PDS-control and PDS-NA), largely due to the fluctuations in the control and NA measurements

Discussion

We found two important differences between the PDS group and the other two groups, confirming one of our hypotheses and rejecting the other. First, the PDS subjects showed a larger decrease in curvature than the others, consistent with previous observation (Pavlin et al. 1996; Adam et al. 2004). Second, the PDS subjects showed a faster anterior motion of the iris (recovering from the initial posterior displacement) than the other two groups, indicating that the chronic posterior bowing of the iris in PDS is not the result of slow recovery. To our knowledge, time-dependent changes in iris curvature following accommodation have not been reported previously. The smaller curvature changes in the NA subjects could be attributed to presbyopia since the group was considerably older, but the differences between the PDS and control groups must be attributed to other causes since the two were age- and correction-matched.

Considerable insight may be drawn from comparison to a previous study of iris contour during sustained prevention of blinking (Liebmann et al. 1995). In that study, as in the current one, steady increase in iris curvature was observed, and the rates were similar. They reported a curvature change of 0.33 mm in 4.4 min , for an average rate of $75 \mu\text{m}/\text{min}$ for the PDS eyes, and a change of 0.1 mm in 2.7 min , for an average rate of $37 \mu\text{m}/\text{min}$ for the control eyes. The similarity in the results – even though there was no initial accommodation event in the previous study and recognizing that the difference was measureable but not statistically significant in the current study – suggests that the underlying mechanism of iris curvature drift is independent of the initial state, and it is consistent with a steady secretion of aqueous humor filling the posterior chamber and pushing the iris forward. As such, it is impossible to distinguish between anterior drift following accommodation in our experiment and the anterior drift previously observed in non-accommodating patients prevented from blinking.

The maximum rate of anterior iris curvature change in our study was $50 \mu\text{m}/\text{min}$ for PDS subjects and $25 \mu\text{m}$ for control and NA subjects. Although the complex geometry and behavior of the posterior chamber during the post-accommodation period makes a precise calculation impossible, an approximation of the volume change due to changes in curvature can be made by means of a simple model based on a series of assumptions:

- The iris root does not move.

- For constant accommodation and pupil diameter, the pupil margin is fixed. In reality, the pupil margin is dynamic even during sustained viewing at a constant distance, but we observed no significant changes in pupil margin position during the post-accommodation period ($p > 0.2$ for all time points vs. each other for all groups), so the simplifying assumption of fixed pupil margin is justified.
- There is negligible motion of the lens during sustained accommodation.
- There is negligible posterior flow of aqueous humor.
- The posterior iris surface is elliptical in shape, and the iris curvature is assumed to represent the semi-minor axis of the ellipse. This assumption lumps all shape changes into a single term, the iris curvature. Although this simplification is consistent with the use of the iris curvature as the sole variable to characterize the shape of the iris, we recognize that complex shape changes could occur and be missed by such an approach (i.e., two different contours could produce the same curvature).

Under the assumptions above, the volume of the posterior chamber changes only due to the forward motion of the midperipheral iris (i.e., increase in curvature), the following simple expression can be derived for the volume change in the posterior chamber as the iris advances (details in Appendix):

$$\frac{\Delta V}{\Delta H} = \frac{\pi^2}{16} (d_{\text{iris}}^2 - d_{\text{pupil}}^2) \quad (1)$$

where ΔV is the change in volume, ΔH is the change in height, d_{iris} is the diameter of the iris, and d_{pupil} is the diameter of the pupil. For an iris diameter of 13 mm and a pupil diameter of 6 mm, the value $\Delta V/\Delta H = 82 \text{ mm}^2 = 0.082 \text{ } \mu\text{L}/\mu\text{m}$. That is, every micron that the iris curvature increases corresponds roughly to 0.082 μL of increased posterior chamber volume. Thus, the 50 $\mu\text{m}/\text{min}$ change in curvature seen in PDS subjects corresponds roughly to a 4.1 $\mu\text{L}/\text{min}$ volume change, and the 25 $\mu\text{m}/\text{min}$ change in curvature seen in non-PDS subjects (control and NA) corresponds roughly to a 2.1 $\mu\text{L}/\text{min}$ volume change.

The calculations above must be considered in light of the aqueous humor secretion rate, which is approximately 2.5 $\mu\text{L}/\text{min}$ (Smith 1991). The volume of the posterior chamber changes as follows:

$$V'_{\text{PC}} = F_{\text{AH}} - F_{\text{PC/AC}} \quad (2)$$

where V'_{PC} is the volume change in the posterior chamber, F_{AH} is the secretion rate of aqueous humor, and $F_{\text{PC/AC}}$ is the net flow from the posterior to the anterior chamber. In the PDS case, the temporary "inversion" of pressure, in which the anterior chamber is at higher pressure than the posterior chamber, is expected to produce a negative $F_{\text{PC/AC}}$ and a large value of V'_{PC} . In the normal and NA cases, $F_{\text{AC/PC}}$ is positive because the posterior chamber is at higher pressure, so V'_{PC} is much lower. Although considerable simplification was made in this analysis – including assuming all iris and pupil diameters to be the same and ignoring posterior outflow in (2) – the basic principles are believed to apply. Of course, it is important to recognize that the 25 $\mu\text{L}/\text{min}$ slope for the NA and control groups was not a particularly good fit, and that the slope was not significantly different from zero (i.e., $F_{\text{PC/AC}}$ could be somewhat larger); at equilibrium, $F_{\text{PC/AC}}$ must be equal to F_{AH} if the posterior outflow pathway is negligible.

Although the difference in recovery rate between the PDS subjects and the others might be explained by the elevated anterior chamber pressure in PDS subjects, the fundamental question of what causes the posterior bowing in PDS remains open.

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Appendix

The derivation of equation (1) is as follows. It is assumed that the only change to posterior chamber volume is due to anterior motion of the iris. That is, the lens and ciliary bodies are assumed stationary, and the pupil diameter is assumed constant. The last assumption is well known to be incorrect – the pupil constricts during dilation – but it is appropriate for a simplified initial analysis. An estimate of posterior chamber volume change with change in iris curvature can then be made by considering the posterior surface of the iris to be a hemi-ellipse with semimajor axis equal to the chord length (i.e., the line connecting the iris root to the pupil margin) and the semiminor axis equal to the line connecting the chord to the posterior iris. The area of the semi-ellipse is given by

$$\begin{aligned} A &= \frac{1}{2}\pi \times (\text{SEMIMAJOR AXIS}) \times (\text{SEMIMINOR AXIS}) \\ &= \frac{1}{2}\pi \times \left(\frac{d_{\text{IRIS}} - d_{\text{PUPIL}}}{4} \right) \times (H) \end{aligned}$$

where H is the iris curvature, and d_{IRIS} and d_{PUPIL} are the iris and pupil diameter. The volume can be calculated using Pappus' Theorem, which states that the volume of a solid of rotation is the area of a slice multiplied by the circumference of the circle traced by the centroid of the slice. Since the centroid of the ellipsoid is located half way between the pupil margin and the iris root, the volume is given by

$$\begin{aligned} V &= A \times \pi \times \left(\frac{d_{\text{PUPIL}} + d_{\text{IRIS}}}{2} \right) \\ &= \frac{1}{2}\pi \times (H) \times \left(\frac{d_{\text{IRIS}} - d_{\text{PUPIL}}}{4} \right) \times \pi \times \left(\frac{d_{\text{PUPIL}} + d_{\text{IRIS}}}{2} \right) \\ &= \frac{1}{16}\pi^2 \times H \times (d_{\text{IRIS}}^2 - d_{\text{PUPIL}}^2) \end{aligned}$$

The iris diameter is assumed unchanged, so the volume is expected to be linear in H with slope as given by equation (1).

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Figure 1. Layout of Study

The test was conducted with the patient lying down with their face slightly turned to the left (a). There was a small mirror mounted on the wall with a target in one corner of the mirror approximately 30–35cm away from the patients eye. In addition, there was a mirror on the opposing wall, 3m away. This second mirror was used to reflect a Snellen chart “E” on the wall above the primary mirror (b). The first image was acquired while the patient was looking at the distant target and the next 4 images were acquired after asking the patient to look at the near target (c).

Figure 2. Calculation of Iris Curvature

The curvature was determined by first drawing a line from the iris root to the most peripheral point of contact between the iris and lens. The longest possible perpendicular line was then drawn from the first line to the iris pigment epithelium. The length of the second line was recorded as the iris curvature, with a positive curvature indicating anterior bowing as seen in this image.

Figure 3. Ultrasound biomicrographs of representative subjects

The iris contour showed relatively little change for control (top row) and narrow angle (middle row) subjects following accommodation, but some increase in curvature over the subsequent three minutes (last column). For the PDS subjects (bottom row), posterior bowing was observed and increased (i.e., the curvature became more negative) after accommodation, followed by recovery over the next three minutes.

Figure 4. Change in iris curvature

Bars show iris curvature in the unaccommodated state (UN) and then 0–3 minutes following accommodation. Normal (black), narrow angle (gray), and pigment dispersion (dotted) groups are shown. Error bars are standard error of the mean.

Figure 5. Rise in curvature following accommodation

Error bars are SEM, and lines are linear regression. PDS: Slope = $49.6 \mu\text{m}/\text{min}$, $R^2 = 0.99$, $p = 0.01$. CONTROL: Slope = $25.4 \mu\text{m}/\text{min}$, $R^2 = 0.69$, $p = 0.14$. NA: Slope = $30.8 \mu\text{m}/\text{min}$, $R^2 = 0.74$, $p = 0.16$.

Table 1Sample groups. Data are mean $\pm$ SD, with range also given for age.

GROUP	N	AGE	M/F	REFRACTIVE ERROR
NARROW ANGLE	16	55 $\pm$ 10 (34–76)	3/13	+1.9 $\pm$ 1.6
PIGMENT DISPERSION	15	40 $\pm$ 15 (12–63)	11/4	–5.1 $\pm$ 2.5
CONTROL	22	37 $\pm$ 12 (20–66)	12/10	–5.0 $\pm$ 2.7